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APPLICATION NO.	F	ILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,044	1,044 07/21/2003		Andrew J. Murphy	REG 780BZ	6377
26693	7590	08/09/2006		EXAMINER	
		RMACEUTICAL	SGAGIAS, MAGDALENE K		
	AW MILL RIVER ROAD WN, NY 10591			ART UNIT	PAPER NUMBER
			1632		
				DATE MAILED: 08/09/2006	

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)					
Office Action Occurrence	10/624,044	MURPHY ET AL.					
Office Action Summary	Examiner	Art Unit					
	Magdalene K. Sgagias	1632					
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondence address					
A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING DA - Extensions of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period w - Failure to reply within the set or extended period for reply will, by statute, Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION 16(a). In no event, however, may a reply be tim rill apply and will expire SIX (6) MONTHS from cause the application to become ABANDONE	I. nely filed the mailing date of this communication. D (35 U.S.C. § 133).					
Status							
1) Responsive to communication(s) filed on 30 M	av 2006						
,	This action is FINAL . 2b) This action is non-final. Since this application is in condition for allowance except for formal matters, prosecution as to the merits is						
closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213.							
closed in accordance with the practice under E	x parte quayle, 1000 C.D. 11, 40	00 0.0. 210.					
Disposition of Claims							
4)⊠ Claim(s) <u>44-47 and 53</u> is/are pending in the application.							
4a) Of the above claim(s) is/are withdrawn from consideration.							
5) Claim(s) is/are allowed.							
6)⊠ Claim(s) <u>44-47 and 53</u> is/are rejected.							
7) Claim(s) is/are objected to.							
8) Claim(s) are subject to restriction and/or	election requirement.						
,	•						
Application Papers							
9) The specification is objected to by the Examiner.							
10) ☐ The drawing(s) filed on is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.							
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).							
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).							
11)☐ The oath or declaration is objected to by the Ex	aminer. Note the attached Office	Action or form PTO-152.					
Priority under 35 U.S.C. § 119							
12) Acknowledgment is made of a claim for foreign a) All b) Some * c) None of: 1. Certified copies of the priority documents 2. Certified copies of the priority documents 3. Copies of the certified copies of the prior application from the International Bureau * See the attached detailed Office action for a list	s have been received. s have been received in Applicati ity documents have been receive (PCT Rule 17.2(a)).	on No ed in this National Stage					
Attachment(s)							
1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)	4) Ll Interview Summary Paper No(s)/Mail Da						
 Notice of Draftsperson's Patent Drawing Review (PTO-948) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7/21/03. 		eatent Application (PTO-152)					

DETAILED ACTION

Claims 44-47 have been amended. New claim 53 has been added. Claims 44-47 and 53 are pending and under consideration.

Response to Arguments

Applicant's arguments, see page 6 of Applicant's response, filed on 05/30/06, with respect to formal objections have been considered and are persuasive. The specification has been amended and hyperlinks have been removed. Claim 52 has been canceled. Therefore, objections have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant's arguments, see page 6 of Applicant's response, filed 05/30/06 with respect to the rejection of claims 44-47 under 35 U.S.C. & 112, first paragraph, for lack of enablement have been fully considered and are persuasive. It is noted that claims 35-39 are withdrawn as claims are canceled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Applicant's arguments, see pages 6-7 of Applicant's response, filed 05/30/06 with respect to the rejection of claims 44-47 under 35 U.S.C. & 112, second paragraph, as indefinite have been fully considered and are persuasive. It is noted that claimed language has been amended to embrace a transgenic mouse containing an endogenous gene locus that has been replaced with and exogenous gene locus. Therefore, rejection of claims 44-47 has been withdrawn.

Applicant's arguments see pages 7-8, filed 05/30/06 with respect to the rejection under 35 U.S.C. & 102(e) have been fully considered but they are not persuasive.

Applicants argue that the present claims are distinguished from the cited patent in numerous respects. First, the transgenic mice discussed by the examiner are relevant only as a means for generating hybridomas that will provide the subject for antibody modification. By contrast, in the present claims the transgenic mice themselves are modified to produce antibodies. Second, the modifications performed in the cited patent on hybridomas are of he rearranged genes encoded by the hybridomas. Such is apparent from the purpose described for modifying variable region (i.e., changing specificity or affinity). Antibody genes do not encode an antibody having any specificity or affinity until they have undergone rearrangement. By contrast the present claims

specify hybrid loci that rearrange during B-cell development. Third, the nature of the modification proposed in the patent is different than that specified in the present claims. The patent proposes changing the affinity or specificity of variable regions not replacing a mouse variable region with a locus, and particularly not such that the human locus is thereby linked to a mouse constant region locus (p7-8).

In response this is not found persuasive because the claimed invention encompass transgenic mice wherein human Ig region loci replace mouse endogenous loci. As such, the rejection of claims 44-47 is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

Art Unit: 1632

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 46 is directed to a transgenic mouse wherein the endogenous immunoglobulin variable region gene locus has been replaced with a homologous or orthologous human variable region gene locus.

The specification has contemplated a transgenic mouse whose genome comprises mouse wherein the endogenous immunoglobulin variable region gene locus has been replaced with a homologous or orthologous human variable region gene locus (p 20). The specification however, has not described any homologous or orthologous human variable region gene locus encompassed by the claims. The instant specification has contemplated the creation of the transgenic mice encompassed by the claims. However, the creation of such is merely a goal of the instant specification, as the claimed mice were not actually made. The evidence of record does not suggest predictability of the existence of the genus of transgenic mice encompassed by the claims. As such the transgenic mice encompassed by the claims and their corresponding phenotypes have not been described by the instant specification.

The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which is not conventional in the art as of applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the

Art Unit: 1632

inventor had possession of the claimed invention. <u>Pfaff v. Wells Electronics, Inc.</u>, 48 USPQ2d 1641, 1646 (1998). However, it would appear that at the time the instant application was filed Applicants were not in possession of the transgenic mice encompassed by the claims, as the instant specification has not reduced to practice such. The skilled artisan cannot envision the detailed chemical structure of the transgenic mice encompassed by the instant claims, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of creating a transgenic mouse. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

The skilled artisan would not recognize that applicant was in possession of the necessary common features or attributes possessed by the genus of transgenic mouse embraced by the claims as such has not been reduced to practice by the instant specification. As such it would appear from the evidence of record that Applicant was not in possession of the genus of transgenic mouse encompassed by the claims.

<u>University of California v. Eli Lilly and Co.</u>, 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Application/Control Number: 10/624,044

Art Unit: 1632

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 44-47 and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Lonberg et al. (U.S. 5,877,397, patented March 2, 1999).

Lonberg et al, teach transgenic mice comprising human lg genes that are introduced into the mouse lg locus by replacing mouse heavy and light immunoglobulin loci directly with fragments of the human heavy and light chain loci using homologous recombination (columns 31-74). Lonberg et al, teach genomic heavy chain human lg transgene (column 31, example 1). Lonberg et al, teach genomic kappa light human lg transgene formed by in vivo homologous recombination (column 32, second example). Lonberg et al, teaches identification of functionally rearranged variable region sequences in transgenic B cells (column 70, example 17).

Thus, claims 44-47 and 53 are anticipated.

Claims 44-47 and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Kucherlapati et al, U.S. Patent 6,114,598, patented September 5, 2000.

Kucherlapati et al, teach transgenic mice comprising human lg genes that are introduced into the mouse lg locus by replacing mouse heavy and light immunoglobulin

Art Unit: 1632

loci directly with fragments of the human heavy and light chain loci using homologous recombination (column 38, lines 16019). Kucherlapati et al, teach replacing human sequences include 100 kb fragment of the human heavy chain region (column 38, lines 23-26). Kucherlapati et al, teach transgenic mice comprising human lg genes that are introduced into the mouse Ig locus by replacing the constant as well as the J region of the kappa locus and replace it with three elements through homologous recombination using regions of homology flanking the constant region (column 25, lines 16-23). Kucherlapati et al, teach transgenic mice comprising human lg genes that are introduced into the mouse Ig locus by replacing the kappa light chain constant (Ck) region (column 22, lines 1-10). Kucherlapati et al, teach transgenic mice producing human monoclonal antibodies in response to immunization (column 39 and 40).

Thus, claims 44-47 and 53 are anticipated.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

Application/Control Number: 10/624,044

Art Unit: 1632

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla, can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Magdalene K. Sgagias, Ph.D. Art Unit 1632

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Page 9